REMARKS

Reconsideration is respectfully requested. Claims 1-3 and 5-85 have been amended. Claims 6, 7, 68 and 69 have been rejected. Claims 1-3, 5, 8-67, and 70-85 have been objected to. Claims 86-89 have been added. Claims 1-3 and 5-89 are now pending.

Applicants reserve the right to pursue in future applications identical or similar claims to those cancelled or amended in this amendment.

Summary of Amendments

Applicants have amended claim 1 to further define R_1 and R_2.

Applicants have amended claim 2 to recite a compound or a mixture of compounds.

Applicants have amended claim 3 to recite compositions comprising a compound formula (I) in which the $-NR_1R_2$ moiety is a ring of formula II or a bicyclic ring system. Support for this amendment may be found for example on page 13, lines 3-12 of the specification (WO 00/47547). Claim 1 has also been amended to recite a compound of formula I.

Applicants have amended claims 5-85 to recite new claim dependencies and reflect the amendments to claims 1, 2 and 3. Claims 19 and 85 have also been amended to include a period at the end of the claim.

Applicants have added claim 86 which recites the limitations of former claim 3.

Applicants have added claim 87 in which the $-NR_1R_2$ moiety of claim 1 is a ring of formula II. Support for this amendment may be found, *e.g.,* on page 13, lines 13-31 of the specification.

Applicants have added claim 88 in which the $-NR_1R_2$ moiety of claim 87 is a substituted or unsubstituted morpholinyl or ketopyrrolidinyl group. Support for this amendment may be found, *e.g.,* on page 14, lines 14-18 of the specification and in the examples.

Applicants have added claim 89 in which the $-NR_1R_2$ moiety of claim 87 is a saturated ring of formula II. Support for this amendment may be found, *e.g.*, on page 14. lines 1-6.

Applicants kindly request consideration of the amendments presented herein. Applicants believe the claims as amended are in condition for allowance and request allowance of claims 1-3 and 5-89.

In the remarks section of Applicants' November 7, 2003 amendment, Applicants stated under the subheading "Summary of Amendments Submitted in this Response" that claims 5-71 and 74-83 were amended to change the term "effective to treat or prevent" to "effective to prevent." Applicants note that this was a typographical error that should have stated that the term "effective to treat or prevent" was changed to "effective to treat."

Petition for Withdrawal for Lack of Unity

Applicants have filed a petition for requesting withdrawal of the improper lack of unity determination. Applicants request favorable consideration of this petition and withdrawal of the lack of unity determination.

Claim Objections

Claims 1-3 and 5-85 have been objected to as containing non-elected subject matter. Applicants respectfully request that the Examiner withdraw the claim rejections.

For the reasons set forth in the response dated November 13, 2003 and the petition for withdrawal of lack of unity that accompanies this response, Applicants respectfully point out that the Examiner fails to meet the requirements for lack of unity. In brief, all compounds in the Markush grouping 1) have a common property or activity, and 2) have a common structure, *i.e.* share a common chemical structure which occupies a large portion of their structures. The Examiner has failed to establish otherwise. Moreover, the Examiner improperly continues to assert that a burden to examination is at all relevant to the determination of lack of unity.

The Examiner is respectfully requested to withdraw the objection to claims 1-85 and withdraw the request that Applicants to limit claim 1 to the subject matter identified by the Examiner.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 6, 7, 68 and 69 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 2 and 5

Applicants respectfully thank the Examiner for noting that the rejection of claims 2 and 5 has been overcome.

Claims 6 and 7

The Examiner rejects claims 6 and 7 as lacking support in the specification for methods of modulating ion channel activity in a warm blooded animal (claim 6) and *in vitro* (claim 7).

Applicants respectfully traverse this rejection. The test of enablement is that one reasonably skilled in the art could make or use the *claimed* invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *See* Manual of Patent Examining Procedures (MPEP), §2164.01. The Examiner has failed to provide any basis (i.e., evidence or reference) to support that one of skill in the art would have been unable to practice the *claimed* methods without "undue experimentation." The Specification provides ample support for the claimed methods. In particular, at page 26 line 21-33 the Specification discloses that the compounds can block ion channels *in vivo* or *in vitro.* At page 38, Example 5 describes assessment of sodium channel blockage in two exemplary compounds. At page 37, Example 4 describes measurement of ECG parameters in rats for the two exemplary compounds. Applicants have thus provided more than sufficient support for the claimed methods. Without a reason to doubt the veracity of Applicants' disclosure, the Specification must be considered enabling.

Applicants are not required to "list diseases related to modulating ion channel activity" or show "treatment of all diseases related to modulating ion channel activity" as alleged by the Examiner. Claims 6 and 7 do not recite any disease states. Applicants are simply required to enable the claims such that one of skill in the art can practice the *claimed invention* without undue experimentation. Applicants respectfully request that the Examiner point to a portion of the MPEP that requires Applicants to enable disease states associated with claimed methods of *in vivo* and *in vitro* methods of modulating enzyme activity, as alleged by the Examiner.

In light of these and other disclosures in the patent application coupled with information known in the art, one reasonably skilled in the art could use the invention of claims 6 and 7 without undue experimentation. Claims 6 and 7 are therefore enabled and Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 112, first paragraph rejections of claims 6 and 7.

Claims 68 and 69

In addition to the above discussion regarding methods of treating arrhythmia and modulating ion channel activity, the Examiner rejects claims 68 and 69 for not having support in the specification for pharmaceutical compositions and methods of treating autoimmune disorders.

Applicants respectfully traverse the rejection. Applicants note that the specification states, *e.g.,* on page 25 that various physiological roles are played by ion channels, that a variety of diseases (including autoimmune disorders, *see* page 30, line 11) are associated with a defective or inadequate function of ion channels, and that compounds which modulate ion channel activity may therefore be useful in the treatment or prevention of autoimmune disorders. In addition, applicants note that one of skill in the art would readily recognize that specific autoimmune diseases that are associated with ion channels. Without a reason to doubt the veracity of the Applicants' disclosure, the Specification must be considered enabling.

Applicants respectfully request that the Examiner withdraw the 35 U.S.C. §112, first paragraph rejection of claims 68 and 69.

Rejection under 35 U.S.C. § 101

The Examiner has maintained the rejection of claims 6 and 7 under 35 U.S.C. § 101. The Examiner contends that claims "6 and 7 are drawn to a mechanism and Applicant has not provided an intended use."

Applicants respectfully traverse this ground for rejection. The initial burden is on the office to establish a *prima facie* case and provide evidentiary support thereof. *See* MPEP § 2107.02. The test for utility before the USPTO is whether the claims have a specific, substantial, and credible utility. *See* MPEP 2107.01. The Examiner has failed to demonstrate that the claims lack a specific, substantial, or credible utility. As such, the Examiner has failed to make a prima facie case for lack of utility.

Moreover, with respect to the Examiner's contention that "the methods are related to a mechanism and Applicants have not provided an intended use," Applicants respectfully assert that only one utility is needed for the claim to meet the requirements of 35 U.S.C. § 101. Multiple utilities for *in vitro* and *in vivo* modulation of ion channels are described in the Specification for the claimed methods, including pharmaceutical testing and treating arrhythmia.

The Examiner is invited to point to the section of the MPEP requiring recitation of specific diseases associated with claimed methods of modulating the activity of a protein to satisfy the utility requirement.

Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 101.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is

determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no.55479-2000500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: August 6, 2004

Respectfully submitted,

By _____

Timothy A. Worrall
Registration No.: 54,552
MORRISON & FOERSTER LLP
425 Market Street
San Francisco, California 94105-2482
(415) 268-7151